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09/757,053

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\*\*\* YOU HAVE NEW MAIL \*\*\*

=> s alpha 2B (2a) adrenergic receptor  
L1 265 ALPHA 2B (2A) ADRENERGIC RECEPTOR

=> s l1 and target  
L2 37 L1 AND TARGET

=> s l2 and ligand  
L3 29 L2 AND LIGAND

=> s alpha 2B (2a) adrenergic receptor?(10a) therap?  
L4 0 ALPHA 2B (2A) ADRENERGIC RECEPTOR?(10A) THERAP?

=> s alpha 2B (2a) adrenergic receptor? (15a) therap?  
L5 1 ALPHA 2B (2A) ADRENERGIC RECEPTOR? (15A) THERAP?

=> d l5 bib abs

L5 ANSWER 1 OF 1 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN  
AN 2002-619081 [66] WPIDS  
DNC C2002-174840  
TI Agent for treating pain such as neuropathic pain comprises a therapeutic  
component and a targeting component.  
DC B04 B05  
IN AOKI, K R; GIL, D W  
PA (ALLR) ALLERGAN SALES INC  
CYC 96  
PI WO 2002053177 A2 20020711 (200266)\* EN 76p  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZM ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU  
SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW  
ADT WO 2002053177 A2 WO 2001-US48651 20011214  
PRAI US 2000-751053 20001229  
AN 2002-619081 [66] WPIDS  
AB WO 200253177 A UPAB: 20021014  
NOVELTY - An agent comprises a therapeutic component (a) and a

09567863

targeting component (b), where the targeting component selectively binds at the **alpha -2B/ alpha -C adrenergic receptor** subtype as compare to the alpha -2A adrenergic receptor subtype.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for making the agent involving producing a polypeptide from a gene having codes for at least one component of the agent.

ACTIVITY - Analgesic; Cytostatic; Antiinflammatory.

MECHANISM OF ACTION - alpha -2B adrenergic receptor binder; Alpha-2B/alpha-2C adrenergic receptor binder.

USE - The novel therapeutic agent is used for treating pain such as chronic pain, visceral pain, neuropathic pain, referred pain and allodynia type pain (persisting from 2 - 27 months) without affecting acute pain sensation or tactile sensation such as chronic pain, visceral pain, neuropathic pain, referred pain and allodynia type pain (claimed) and for treating pain associated with cancer and irritable bowel syndrome.

ADVANTAGE - (b) selectively binds at the alpha -2B or alpha -2B/ alpha 2B- alpha -2C adrenergic receptor subtypes(s) as compared to the alpha -2A adrenergic receptor subtype. (a) inactivates cellular ribosomes. Dwg.0/1

=> s alpha 2B (2a) adrenergic receptor? (20a) ligand?  
L6 13 ALPHA 2B (2A) ADRENERGIC RECEPTOR? (20A) LIGAND?

=> s l6 not l5  
L7 13 L6 NOT L5

=> dup rem l7  
PROCESSING COMPLETED FOR L7  
L8 8 DUP REM L7 (5 DUPLICATES REMOVED)

=> d l8 bib abs 1-8

L8 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN  
AN 2002:521523 CAPLUS  
DN 137:73273  
TI Adrenergic receptor ligand-neurotoxin conjugates and methods for treating pain  
IN Gil, Daniel W.; Aoki, Kei Roger  
PA Allergan Sales, Inc., USA  
SO PCT Int. Appl., 76 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002053177	A2	20020711	WO 2001-US48651	20011214
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2000-751053	A	20001229		

OS MARPAT 137:73273

AB Agents for treating pain, methods for producing the agents, and methods for treating pain by administration to a patient of a therapeutically

effective amt. of the agent, are disclosed. The agent may include a clostridial neurotoxin, a fragment or a deriv. thereof, attached to a targeting component, wherein the targeting component is selected from a group consisting of compds. which selectively binds at the .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptor subtype(s) as compared to other binding sites, e.g. the .alpha.2a adrenergic receptor subtype.

L8 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2002:213371 CAPLUS  
 DN 137:138464  
 TI Gender difference in diet-induced obesity hypertension: implication of renal .alpha.2-adrenergic receptors  
 AU Coatmellec-Taglioni, Gwenn; Dausse, Jean-Pierre; Giudicelli, Yves; Ribiere, Catherine  
 CS Department of Biochemistry and Molecular Biology, Universite Rene Descartes, Paris, Fr.  
 SO American Journal of Hypertension (2002), 15(2, Pt. 1), 143-149  
 CODEN: AJHYE6; ISSN: 0895-7061  
 PB Elsevier Science Inc.  
 DT Journal  
 LA English  
 AB Although the pathogenesis of the obesity-related hypertension is not fully understood, prevalence of the cardiovascular complications is much higher in obese men than obese women. In a recent study, we reported that male rats fed a cafeteria diet, while becoming obese, developed hypertension and important changes in their renal .alpha.2-adrenergic receptor subtypes distributions. The aim of the present study was to investigate whether these alterations are sex dependent. After 10 wk of the cafeteria diet, male and female rats had the same increase in fat pad wt. and in plasma leptin levels. However, in contrast to males, females had normal blood pressure (BP). On the basis of radioligand-binding studies using [3H]-RX821002 and confirming our recent observation, an increase in .alpha.2-adrenergic receptor densities occurred in kidneys of cafeteria-fed male but not female rats. Moreover, in contrast with the situation obsd. in males, ligand competition studies failed to reveal any change in the renal .alpha.2A-and .alpha.2B -adrenergic receptors subtypes distribution in females. Finally, in the cafeteria-fed females reverse transcription-polymerase chain reaction expts. showed unaltered expression of these two .alpha.2-adrenergic receptor subtypes. These data thus suggest a strong relationship between the sexual dimorphism in the cafeteria diet-induced hypertension and altered expression of the .alpha.2-adrenergic receptor subtypes in the kidney.  
 RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 1  
 AN 1997-107576 [10] WPIDS  
 CR 1991-310087 [42]  
 DNC C1997-034339  
 TI Assay for alpha-2b adrenergic receptor ligands - using membranes of cells expressing recombinant receptor.  
 DC B04 D16  
 IN HARTIG, P R; WEINSHANK, R L  
 PA (SYNA-N) SYNAPTIC PHARM CORP  
 CYC 1  
 PI US 5595880 A 19970121 (199710)\* 16p  
 ADT US 5595880 A Div ex US 1989-428856 19891030, Cont of US 1991-707604 19910530, US 1992-965040 19921022  
 FDT US 5595880 A Div ex US 5053337  
 PRAI US 1989-428856 19891030; US 1991-707604 19910530; US 1992-965040

09567863

19921022

AN 1997-107576 [10] WPIDS

CR 1991-310087 [42]

AB US 5595880 A UPAB: 19970307

A novel method for determining if a cpd. specifically binds to human alpha 2b adrenergic receptor comprises: (a) obtaining a membrane prepn. from mammalian cells which contain an isolated nucleic acid mol. encoding the receptor and which express the encoded receptor on their cell surface; (b) contacting the cpd. with the membrane prepn. under conditions that permit binding of the cpd. to the receptor; and (c) detecting any such binding.

USE - The method may be used to screen for alpha 2b receptor ligands as potential drugs.

Dwg.0/4

L8 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 1991:331010 BIOSIS

DN BR41:27560

TI MONOVALENT CATION AND AMILORIDE ANALOG MODULATION OF ADRENERGIC  
**LIGAND BINDING TO THE UNGLYCOSYLATED ALPHA-2B-  
ADRENERGIC RECEPTOR ALPHA-2B-AR  
SUBTYPE.**

AU WILSON A L; SEIBERT K; BRANDON S; CRAGOE E J JR; LIMBIRD L E

CS DEP. PHARMACOL., VANDERBILT UNIV. SCH. MED., NASHVILLE, TENN. 37232.

SO 75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR  
EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED  
AM SOC EXP BIOL) J. (1991) 5 (6), A1584.

CODEN: FAJOEC. ISSN: 0892-6638.

DT Conference

FS BR; OLD

LA English

L8 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 2

AN 1991:276175 BIOSIS

DN BA92:8790

TI MONOVALENT CATION AND AMILORIDE ANALOG MODULATION OF ADRENERGIC  
**LIGAND BINDING TO THE UNGLYCOSYLATED ALPHA-2B-  
ADRENERGIC RECEPTOR SUBTYPE.**

AU WILSON A L; SEIBERT K; BRANDON S; CRAGOE E J JR; LIMBIRD L E

CS DEP. PHARMACOL., VANDERBILT UNIV., SCH. MED., NASHVILLE, TENN. 37232-6600.

SO MOL PHARMACOL, (1991) 39 (4), 481-486.

CODEN: MOPMA3. ISSN: 0026-895X.

FS BA; OLD

LA English

AB The unglycosylated .alpha.2B subtype of the .alpha.2-adrenergic receptor found in NG-108-15 cells possesses allosteric regulation of adrenergic ligand binding by monovalent cations and 5-amino-substituted amiloride analogs. These findings demonstrate that allosteric modulation of adrenergic ligand binding is not a property unique to the .alpha.2A subtype. The observation that amiloride analogs as well as monovalent cation can modulate adrenergic ligand binding to the nonglycosylated .alpha.2B subtype indicates that charge shielding due to carbohydrate moieties does not play a role in this allosteric modulation but, rather, these regulatory effects result from interactions of cations and amiloride analogs with the protein moiety of the receptor. Furthermore, the observation that both .alpha.2A and .alpha.2B receptor subtypes are modulated by amiloride analogs suggests that structural domains that are conserved between the two are likely to be involved in this allosteric modulation.

L8 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 1991:504672 BIOSIS

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DN BA92:127632  
TI PHARMACOLOGICAL CHARACTERIZATION OF RAT ALPHA-2-ADRENERGIC RECEPTORS.  
AU HARRISON J K; D'ANGELO D D; ZENG D; LYNCH K R  
CS DEP. PHARMACOLOGY, BOX 448, UNIVERSITY VIRGINIA SCH. MED., 1300 JEFFERSON  
PARK AVE., CHARLOTTESVILLE, VA. 22908.  
SO MOL PHARMACOL, (1991) 40 (3), 407-412.  
CODEN: MOPMA3. ISSN: 0026-895X.  
FS BA; OLD  
LA English  
AB We described previously the molecule characterization of a rat .  
**alpha.2B-adrenergic receptor** and  
have shown also that the rat genome contains three closely related  
.alpha.2-adrenergic receptor genes. To characterize the **ligand**  
-binding properties of these receptor gene products, we expressed the DNAs  
encoding these receptors individually in COS-1 cells and studied their  
binding to a wide variety of typical and atypical adrenergic lgands. The  
receptors displayed high affinity binding to the radioligand  
[3H]rauwolscine, with equilibrium dissociation constants ranging from 1.4  
to 28 nM. Kinetic analysis of the binding of [3H]rauwolscine to membranes  
from transfected cells was in very good agreement with data obtained from  
saturation analysis. We examined the ability of a number of agents to  
compete for the binding of [3]rauwolscine to the .alpha.2-adrenergic  
receptor-transfected membranes. Whereas one of these receptors displayed a  
pharmacological profile typical of an .alpha.2A-adrenergic receptor, the  
other two receptors showed similar pharmacological properties  
characteristic of an .alpha.2B-adrenergic receptor. The two .alpha.2B-like  
adrenergic receptors differed, however, in the ratios of Ki values for  
oxymetazoline and prazosin, as well as the Ki ratio of prazosin and  
yohimbine. In addition, the two .alpha.2B-like adrenergic receptors had a  
9-fold difference in affinity for chlorpromazine. The pharmacological  
characterization of the three rat .alpha.2-adrenergic receptor gene  
products is consistent with the known pharmacology of .alpha.2-adrenergic  
receptors, as documented using tissues and cell lines.

L8 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 3  
AN 1988:503728 BIOSIS  
DN BA86:124412  
TI CLONING AND EXPRESSION OF A HUMAN KIDNEY COMPLEMENTARY DNA FOR AN  
ALPHA-2-ADRENERGIC RECEPTOR SUBTYPE.  
AU REGAN J W; KOBILKA T S; YANG-FENG T L; CARON M G; LEFKOWITZ R J; KOBILKA B  
K  
CS HOWARD HUGHES MED. INST., DUKE UNIV. MED. CENT., DURHAM, N.C. 27710.  
SO PROC NATL ACAD SCI U S A, (1988) 85 (17), 6301-6305.  
CODEN: PNASA6. ISSN: 0027-8424.  
FS BA; OLD  
LA English  
AB An .alpha.2-adrenergic receptor subtype has been cloned from a human  
kidney cDNA library using the gene for the human platelet  
.alpha.2-adrenergic receptor as a probe. The deduced amino acid sequence  
resembles the human platelet .alpha.2-adrenergic receptor and is  
consistent with the structure of other members of the family of guanine  
nucleotide-binding protein-coupled receptors. The cDNA was expressed in a  
mammalian cell line (COS-7), and the .alpha.2-adrenergic **ligand**  
[3H]rauwolscine was bound. Competition curve analysis with a variety of  
adrenergic ligands suggests that this cDNA clone represents the  
**.alpha.2B-adrenergic receptor**. The  
gene for this receptor is on human chromosome 4, whereas the gene for the  
human platelet .alpha.2-adrenergic receptor (.alpha.2A) lies on chromosome  
10. This ability to express the receptor in mammalian cells, free of other  
adrenergic receptor subtypes, should help in developing more selective  
.alpha.-adrenergic ligands.

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L8 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN  
AN 1988:417541 CAPLUS  
DN 109:17541  
TI Alpha-2A and alpha-2B adrenergic receptor subtypes: antagonist binding in  
tissues and cell lines containing only one subtype  
AU Bylund, David B.; Ray-Prenger, Carla; Murphy, T. J.  
CS Sch. Med., Univ. Missouri, Columbia, MO, 65212, USA  
SO Journal of Pharmacology and Experimental Therapeutics (1988), 245(2),  
600-7  
CODEN: JPETAB; ISSN: 0022-3565  
DT Journal  
LA English  
AB The affinities of 34 adrenergic antagonists for .alpha.2-adrenergic  
receptors were detd. from homogenate radioligand binding studies with  
[3H]yohimbine and [3H]rauwolscine. It has been suggested that  
.alpha.2-adrenergic receptors can be subdivided into .alpha.2A and  
.alpha.2B subtypes. Oxymetazoline is selective for .alpha.2A receptors,  
whereas prazosin is .alpha.2B selective. Five different tissues were  
used, each of which has only 1 of the 2 subtypes: human platelets  
(.alpha.2A), the HT29 cell line (.alpha.2A), human cerebral cortex  
(.alpha.2A), neonatal rat lung (.alpha.2B), and NG108-15 cell line  
(.alpha.2B). The drug affinities were highly correlated when .alpha.2A  
tissues were compared with .alpha.2A tissues ( $r = 0.97-0.98$ ) or when the 2  
.alpha.2B tissues were compared ( $r = 0.99$ ). By contrast, comparison of an  
.alpha.2A tissue with an .alpha.2B tissue resulted in poor correlations ( $r$   
 $= 0.77$  to  $-0.87$ ). Three new subtype-selective drugs were identified among  
these drugs on the basis of at least a 10-fold greater affinity for 1  
subtype. All 3 were selective for the .alpha.2B subtype: ARC-239  
(100-fold selective), chlorpromazine (18-fold selective), and  
7-hydroxychlorpromazine (17-fold selective). These studies, by  
demonstrating distinct pharmacol. profiles for the 2 .alpha.2-adrenergic  
receptor subtypes in several different tissues, further support the  
existence and definition of these subtypes. The identification of a cell  
line for each subtype should be useful in the further study of  
.alpha.2-adrenergic receptor subtypes.

=> d 18 3 kwic

L8 ANSWER 3 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 1  
TI Assay for alpha-2b adrenergic  
receptor ligands - using membranes of cells expressing  
recombinant receptor.

=>

Connection closed by remote host

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FILE 'HOME' ENTERED AT 13:16:58 ON 10 SEP 2003

=> file biosis medline caplus wpids uspatfull  
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\*\*\* YOU HAVE NEW MAIL \*\*\*

=> s saporin and imiloxan  
L1 4 SAPORIN AND IMILOXAN

=> s l1 and adrenergic receptor?  
L2 0 L1 AND ADRENERGIC RECEPTOR?

=> s saporin and adrenergic receptor  
L3 189 SAPORIN AND ADRENERGIC RECEPTOR

=> s l3 and prazosin  
L4 2 L3 AND PRAZOSIN

=> d l4 bib abs 1-2

L4 ANSWER 1 OF 2 MEDLINE on STN  
AN 2002147402 MEDLINE  
DN 21676103 PubMed ID: 11818770  
TI Isoflurane and nociception: spinal alpha2A adrenoceptors mediate  
antinociception while supraspinal alpha1 adrenoceptors mediate  
pronociception.  
AU Kingery Wade S; Agashe Geeta S; Guo Tian Z; Sawamura Shigehito; Davies M  
Frances; Clark J David; Kobilka Brian K; Maze Mervyn  
CS Department of Anesthesia, Stanford University, Stanford, California, USA.  
NC 30232  
SO ANESTHESIOLOGY, (2002 Feb) 96 (2) 367-74.  
Journal code: 1300217. ISSN: 0003-3022.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals  
EM 200204  
ED Entered STN: 20020308  
Last Updated on STN: 20020404  
Entered Medline: 20020402  
AB BACKGROUND: The authors recently established that the analgesic actions of  
the inhalation anesthetic nitrous oxide were mediated by noradrenergic



bulbospinal neurons and spinal alpha2B adrenoceptors. They now determined whether noradrenergic brainstem nuclei and descending spinal pathways are responsible for the antinociceptive actions of the inhalation anesthetic isoflurane, and which alpha adrenoceptors mediate this effect. METHODS: After selective lesioning of noradrenergic nuclei by intracerebroventricular application of the mitochondrial toxin **saporin** coupled to the antibody directed against dopamine beta hydroxylase (DbetaH-**saporin**), the antinociceptive action of isoflurane was determined. Antagonists for the alpha1 and alpha2 adrenoceptors were injected at spinal and supraspinal sites in intact and spinally transected rats to identify the noradrenergic pathways mediating isoflurane antinociception. Null mice for each of the three alpha2-adrenoceptor subtypes (alpha2A, alpha2B, and alpha2C) and their wild-type cohorts were tested for their antinociceptive response to isoflurane. RESULTS: Both DbetaH-**saporin** treatment and chronic spinal transection enhanced the antinociceptive effects of isoflurane. The alpha1-adrenoceptor antagonist **prazosin** also enhanced isoflurane antinociception at a supraspinal site of action. The alpha2-adrenoceptor antagonist yohimbine inhibited isoflurane antinociception, and this effect was mediated by spinal alpha2 adrenoceptors. Null mice for the alpha2A-adrenoceptor subtype showed a reduced antinociceptive response to isoflurane. CONCLUSIONS: The authors suggest that, at clinically effective concentrations, isoflurane can modulate nociception via three different mechanisms: (1) a pronociceptive effect requiring descending spinal pathways, brainstem noradrenergic nuclei, and supraspinal alpha1 adrenoceptors; (2) an antinociceptive effect requiring descending noradrenergic neurons and spinal alpha2A adrenoceptors; and (3) an antinociceptive effect mediated within the spinal cord for which no role for adrenergic mechanism has been found.

L4 ANSWER 2 OF 2 USPATFULL on STN

AN 2003:231628 USPATFULL

TI Polymeric immunoglobulin fusion proteins that target low-affinity fcyreceptors

IN Arnason, Barry G. W., Chicago, IL, UNITED STATES

Jensen, Mark A., Chicago, IL, UNITED STATES

White, David M., Chicago, IL, UNITED STATES

PA The University of Chicago (U.S. corporation)

PI US 2003161826 A1 20030828

AI US 2002-96521 A1 20020311 (10)

PRAI US 2001-274392P 20010309 (60)

DT Utility

FS APPLICATION

LREP Mark B. Wilson, Fulbright & Jaworski L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX, 78701

CLMN Number of Claims: 82

ECL Exemplary Claim: 1

DRWN 7 Drawing Page(s)

LN.CNT 4867

AB The present invention concerns a family of nucleic acids, polypeptides and cloning vectors which direct expression of fusion proteins that can mimic aggregated IgG (AIG) and immune complex function with respect to their interactions with Fc.gamma.R and which allow for the inclusion and targeting of a second protein domain to cells expressing Fc.gamma.R. This was accomplished by expressing multiple linear copies of the hinge and CH2 domains (HCH2) of human IgG.sub.1 fused to the framework region of human IgG.sub.1. Convenient restriction sites allow for the facile introduction of additional amino-terminal domains. Methods for treating patients using fusion proteins are also disclosed. The HCH2 polymers described here represent a new strategy in the design of recombinant proteins for the therapeutic targeting of Fc.gamma.R in autoimmune disorders.

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=> s l1 and adren? (4a) receptor?

L5 0 L1 AND ADREN? (4A) RECEPTOR?

=> s therap? and adren? (4a) receptor?

L6 13375 THERAP? AND ADREN? (4A) RECEPTOR?

=> s l6 and alpha? (5a) subtype?

L7 665 L6 AND ALPHA? (5A) SUBTYPE?

=> s l7 and target?

L8 329 L7 AND TARGET?

=> s l8 and target? (5a) bind? (5a) alpha?

L9 1 L8 AND TARGET? (5A) BIND? (5A) ALPHA?

=> d l9 bib abs

L9 ANSWER 1 OF 1 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2002-619081 [66] WPIDS

DNC C2002-174840

TI Agent for treating pain such as neuropathic pain comprises a **therapeutic** component and a **targeting** component.

DC B04 B05

IN AOKI, K R; GIL, D W

PA (ALLR) ALLERGAN SALES INC

CYC 96

PI WO 2002053177 A2 20020711 (200266)\* EN 76p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU  
SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

ADT WO 2002053177 A2 WO 2001-US48651 20011214

PRAI US 2000-751053 20001229

AN 2002-619081 [66] WPIDS

AB WO 200253177 A UPAB: 20021014

NOVELTY - An agent comprises a **therapeutic** component (a) and a **targeting** component (b), where the **targeting** component selectively **binds** at the **alpha -2B/ alpha -C adrenergic receptor subtype** as compare to the **alpha -2A adrenergic receptor subtype**

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for making the agent involving producing a polypeptide from a gene having codes for at least one component of the agent.

ACTIVITY - Analgesic; Cytostatic; Antiinflammatory.

MECHANISM OF ACTION - **alpha -2B adrenergic receptor binder; Alpha-2B/alpha-2C adrenergic receptor binder.**

USE - The novel **therapeutic** agent is used for treating pain such as chronic pain, visceral pain, neuropathic pain, referred pain and allodynia type pain (persisting from 2 - 27 months) without affecting acute pain sensation or tactile sensation such as chronic pain, visceral pain, neuropathic pain, referred pain and allodynia type pain (claimed) and for treating pain associated with cancer and irritable bowel syndrome.

ADVANTAGE - (b) selectively binds at the **alpha -2B or alpha -2B/ alpha 2B- alpha -2C adrenergic receptor subtypes(s)** as compared to the **alpha -2A adrenergic receptor subtype. (a)**

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inactivates cellular ribosomes.  
Dwg.0/1

=>

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=> d his

(FILE 'HOME' ENTERED AT 13:16:58 ON 10 SEP 2003)

FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 13:17:21 ON 10 SEP 2003

L1 4 S SAPORIN AND IMILOXAN  
L2 0 S L1 AND ADRENERGIC RECEPTOR?  
L3 189 S SAPORIN AND ADRENERGIC RECEPTOR  
L4 2 S L3 AND PRAZOSIN  
L5 0 S L1 AND ADREN? (4A) RECEPTOR?  
L6 13375 S THERAP? AND ADREN? (4A) RECEPTOR?  
L7 665 S L6 AND ALPHA? (5A) SUBTYPE?  
L8 329 S L7 AND TARGET?  
L9 1 S L8 AND TARGET? (5A) BIND? (5A) ALPHA?

=> s l8 and target? (7a) alpha?

L10 122 L8 AND TARGET? (7A) ALPHA?

=> s l10 and prazosin

L11 66 L10 AND PRAZOSIN

=> s l11 and arc 239

L12 2 L11 AND ARC 239

=> d l12 bib abs 1-2

L12 ANSWER 1 OF 2 USPATFULL on STN  
AN 2003:165870 USPATFULL  
TI Alpha-2 **adrenergic receptor** polymorphisms  
IN Small, Kersten M., Cincinnati, OH, UNITED STATES  
Liggett, Stephen B., Cincinnati, OH, UNITED STATES  
PI US 2003113725 A1 20030619  
AI US 2001-1073 A1 20011101 (10)  
RLI Continuation-in-part of Ser. No. US 2000-551744, filed on 17 Apr 2000,  
PENDING Continuation-in-part of Ser. No. US 2000-636259, filed on 10 Aug  
2000, PENDING Continuation-in-part of Ser. No. US 2000-692077, filed on  
19 Oct 2000, PENDING  
PRAI WO 2001-US12575 20010417  
DT Utility  
FS APPLICATION  
LREP Holly D. Kozlowski, Dinsmore & Shohl LLP, 1900 Chemed Center, 255 East  
Fifth Street, Cincinnati, OH, 45202  
CLMN Number of Claims: 17  
ECL Exemplary Claim: 1  
DRWN 15 Drawing Page(s)  
LN.CNT 4834  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The present invention includes polymorphisms in nucleic acids encoding  
the alpha-2B, alpha-2A, and alpha-2C **adrenergic**  
**receptor** and expressed alpha-2B, alpha-2A and alpha-2C  
**adrenergic receptor** molecule. The invention also  
pertains to methods and molecules for detecting such polymorphisms. The  
invention further pertains to the use of such molecules and methods in  
the diagnosis, prognosis, and treatment of diseases such as  
cardiovascular and central nervous system disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 2 OF 2 USPATFULL on STN .

AN 2001:139296 USPATFULL

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TI DNA molecule encoding a variant alpha2B-adrenoceptor protein, and uses thereof

IN Snapir, Amir, Turku, Finland  
Heinonen, Paula, Turku, Finland  
Alhopuro, Pia, Turku, Finland  
Karvonen, Matti, Turku, Finland  
Koulu, Markku, Turku, Finland  
Pesonen, Ullamari, Turku, Finland  
Scheinin, Mika, Naantali, Finland  
Salonen, Jukka T., Jannevirta, Finland  
Tuomainen, Tomi-Pekka, Kuopio, Finland  
Lakka, Timo A., Kuopio, Finland  
Nyyssönen, Kristiina, Kuopio, Finland  
Salonen, Riitta, Jannevirta, Finland  
Kauhanen, Jussi, Kuopio, Finland  
Valkonen, Veli-Pekka, Kuopio, Finland

PA OY Juvantia Pharma Ltd., Turku, Finland (non-U.S. corporation)

PI US 2001016338 A1 20010823

AI US 2001-825923 A1 20010405 (9)

RLI Division of Ser. No. US 1999-422985, filed on 22 Oct 1999, PENDING

DT Utility

FS APPLICATION

LREP ROTHWELL, FIGG, ERNST & MANBECK, P.C., 555 13TH STREET, N.W., SUITE 701, EAST TOWER, WASHINGTON, DC, 20004

CLMN Number of Claims: 26

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 989

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to a DNA sequence comprising a nucleotide sequence encoding a variant .alpha..sub.2B-adrenoceptor protein and to said variant .alpha..sub.2B-adrenoceptor protein as well as a method for screening a subject to determine if said subject is a carrier of a variant gene that encodes said variant .alpha..sub.2B-adrenoceptor. Further this invention relates to a method for treating a mammal suffering from vascular contraction of coronary arteries, said method comprising the step of administering a selective .alpha..sub.2B-adrenoceptor antagonist to said mammal and to transgenic animals comprising a human DNA molecule encoding human .alpha..sub.2B-adrenoceptor or said variant .alpha..sub.2B-adrenoceptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> s 119 and alpha (3a) 2B  
L20 11 L19 AND ALPHA (3A) 2B

=> dup rem 120  
PROCESSING COMPLETED FOR L20  
L21 11 DUP REM L20 (0 DUPLICATES REMOVED)

=> d 121 bib abs 1-11

L21 ANSWER 1 OF 11 USPATFULL on STN  
AN 2003:140965 USPATFULL  
TI Arthroscopic irrigation solution and method for peripheral  
vasoconstriction and inhibition of **pain** and inflammation  
IN Demopulos, Gregory A., Mercer Island, WA, UNITED STATES  
Palmer, Pamela Pierce, San Francisco, CA, UNITED STATES  
Herz, Jeffery M., Mill Creek, WA, UNITED STATES  
PA Omeros Corporation (U.S. corporation)  
PI US 2003096807 A1 20030522  
AI US 2002-138192 A1 20020501 (10)  
RLI Continuation-in-part of Ser. No. US 2001-839633, filed on 20 Apr 2001,  
PENDING Continuation-in-part of Ser. No. WO 1999-US24672, filed on 20  
Oct 1999, UNKNOWN  
PRAI US 1998-105029P 19981020 (60)  
DT Utility  
FS APPLICATION  
LREP OMEROS MEDICAL SYSTEMS, INC., 1420 FIFTH AVENUE, SUITE 2675, SEATTLE,  
WA, 98101  
CLMN Number of Claims: 105  
ECL Exemplary Claim: 1  
DRWN 3 Drawing Page(s)  
LN.CNT 3576  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB A method and solution for perioperatively inhibiting a variety of  
**pain** and inflammation processes during arthroscopic procedures.  
The solution preferably includes a vasoconstrictor that exhibits  
alpha-adrenergic activity and one or more additional **pain** and  
inflammation inhibitory agents at dilute concentration in a physiologic  
carrier, such as saline or lactated Ringer's solution. The solution is  
applied by continuous irrigation of a wound during a surgical procedure  
for peripheral vasoconstriction and inhibition of **pain** and/or  
inflammation while avoiding undesirable side effects associated with  
systemic application of larger doses of the agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 2 OF 11 USPATFULL on STN  
AN 2003:127747 USPATFULL  
TI Arthroscopic irrigation solution and method for peripheral  
vasoconstriction and inhibition of **pain** and inflammation  
IN Demopulos, Gregory A., Mercer Island, WA, UNITED STATES  
Palmer, Pamela Pierce, San Francisco, CA, UNITED STATES  
Herz, Jeffery M., Mill Creek, WA, UNITED STATES  
PA Omeros Corporation (U.S. corporation)  
PI US 2003087962 A1 20030508  
AI US 2002-138193 A1 20020501 (10)  
RLI Continuation-in-part of Ser. No. US 2001-839633, filed on 20 Apr 2001,  
PENDING Continuation-in-part of Ser. No. WO 1999-US24672, filed on 20  
Oct 1999, UNKNOWN  
PRAI US 1998-105029P 19981020 (60)

09567863

DT Utility  
FS APPLICATION  
LREP OMEROS MEDICAL SYSTEMS, INC., 1420 FIFTH AVENUE, SUITE 2675, SEATTLE,  
WA, 98101  
CLMN Number of Claims: 54  
ECL Exemplary Claim: 1  
DRWN 3 Drawing Page(s)  
LN.CNT 3339

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and solution for perioperatively inhibiting a variety of  
**pain** and inflammation processes during arthroscopic procedures.  
The solution preferably includes a vasoconstrictor that demonstrates  
substantial agonist activity at alpha adrenergic receptors and that is  
selected for peripheral (local) vasoconstriction and one or more  
additional **pain** and inflammation inhibitory agents at dilute  
concentration in a physiologic carrier, such as saline or lactated  
Ringer's solution. The solution is applied by continuous irrigation of a  
wound during a surgical procedure for peripheral vasoconstriction and  
inhibition of **pain** and/or inflammation while avoiding  
undesirable side effects associated with systemic application of larger  
doses of the agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 3 OF 11 USPATFULL on STN  
AN 2003:51589 USPATFULL  
TI Yohimbine dimers exhibiting **binding** selectivities for  
**alpha2** adrenergic **receptors**  
IN Miller, Duane D., Germantown, TN, UNITED STATES  
Zheng, Weiping, Baltimore, MD, UNITED STATES  
Moore, Bob M., II, Nesbit, MS, UNITED STATES  
Mustafa, Suni, Memphis, TN, UNITED STATES  
PI US 2003036547 A1 20030220  
AI US 2002-106521 A1 20020325 (10)  
PRAI US 2001-278181P 20010323 (60)  
DT Utility  
FS APPLICATION  
LREP Michael L. Goldman, NIXON PEABODY LLP, Clinton Square, P.O. Box 31051,  
Rochester, NY, 14603-1051  
CLMN Number of Claims: 48  
ECL Exemplary Claim: 1  
DRWN 1 Drawing Page(s)  
LN.CNT 1401

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to yohimbine dimer compounds,  
pharmaceutical compositions containing such dimer compounds, methods of  
making such dimer compounds, and uses thereof. The yohimbine dimer  
compounds include compounds of formula (I): ##STR1##

where R is any linker molecule which affords a yohimbine dimer that has  
activity as an .alpha..sub.2-AR antagonist and has selectivity for an  
.alpha..sub.2-AR subtype over another .alpha..sub.2-AR subtype.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN  
AN 2002:754163 CAPLUS  
DN 137:263224  
TI Yohimbine dimers exhibiting **binding** selectivities for .  
**alpha.2** adrenergic **receptors**  
IN Miller, Duane D.; Zheng, Weiping; Moore, Robert M., II; Mustafa, Suni  
PA The University of Tennessee Research Corporation, USA

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SO PCT Int. Appl., 43 pp.

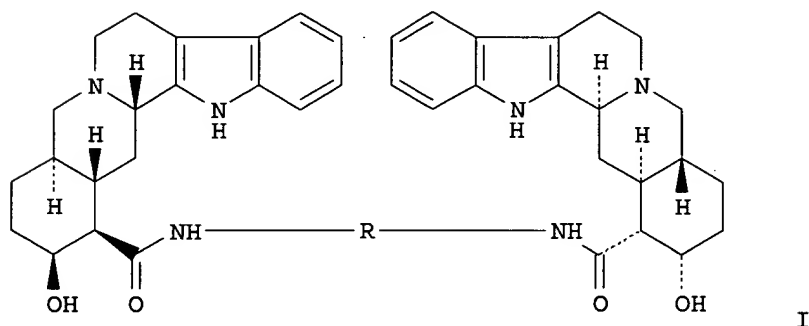
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002076399	A2	20021003	WO 2002-US9267	20020325
	WO 2002076399	A3	20021114		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2003036547	A1	20030220	US 2002-106521	20020325
PRAI	US 2001-278181P	P	20010323		
OS	MARPAT 137:263224				
GI					



AB The yohimbine dimer compds. I (R = linker mol. having a length of 2.5 .ANG. to about 45 .ANG.) were prepd. as an .alpha.2-AR antagonist and has selectivity of an .alpha.2 -AR subtype over another .alpha.2-AR subtype. Thus, yohimbinic acid was treated with H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> to give I (R = CH<sub>2</sub>CH<sub>2</sub>).HCl. The binding affinity (K<sub>i</sub>) of I (R = CH<sub>2</sub>CH<sub>2</sub>).HCl on human .alpha.2a-AR was 26.4 .+- . 7.3 and .alpha.2b-AR was 1510 .+- . 262 with a .alpha.2a/.alpha.2b selectivity of 57.2.

L21 ANSWER 5 OF 11 USPATFULL on STN

AN 2002:228338 USPATFULL

TI Piperidine-piperazine ligands for neurotransmitter receptors

IN Persons, Paul E., Westborough, MA, UNITED STATES

Radeke, Heike, South Grafton, MA, UNITED STATES

PI US 2002123499 A1 20020905

AI US 2002-87609 A1 20020301 (10)

PRAI US 2001-272966P 20010302 (60)

DT Utility

FS APPLICATION

LREP FOLEY HOAG LLP, PATENT GROUP, 155 SEAPORT BOULEVARD, BOSTON, MA, 02110

CLMN Number of Claims: 83



09567863

ECL Exemplary Claim: 1

DRWN 6 Drawing Page(s)

LN.CNT 2808

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB One aspect of the present invention relates to piperidine-piperazine compounds. A second aspect of the present invention relates to the use of the piperidine-piperazine compounds as ligands for various mammalian cellular receptors or transporters or both, including dopamine, serotonin or norepinephrine receptors or transporters, any combination of them, or all of them. The compounds of the present invention will find use in the treatment of numerous ailments, conditions and diseases which afflict mammals, including but not limited to addiction, anxiety, depression, sexual dysfunction, hypertension, migraine, Alzheimer's disease, obesity, emesis, psychosis, analgesia, schizophrenia, Parkinson's disease, restless leg syndrome, sleeping disorders, attention deficit hyperactivity disorder, irritable bowel syndrome, premature ejaculation, menstrual dysphoria syndrome, urinary incontinence, inflammatory **pain**, neuropathic **pain**, Lesche-Nyhan disease, Wilson's disease, and Tourette's syndrome. An additional aspect of the present invention relates to the synthesis of combinatorial libraries of the piperidine-piperazine compounds, and the screening of those libraries for biological activity, e.g., in assays based on dopamine receptors or transporters or both.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 6 OF 11 USPATFULL on STN

AN 2002:99464 USPATFULL

TI Selective anxiolytic therapeutic agents

IN Hanns, Mohler, Meilen, SWITZERLAND

Rudolph, Uwe, Zurich, SWITZERLAND

PI US 2002052365 A1 20020502

AI US 2001-972799 A1 20011005 (9)

PRAI US 2000-238189P 20001005 (60)

DT Utility

FS APPLICATION

LREP PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711

CLMN Number of Claims: 18

ECL Exemplary Claim: 1

DRWN 4 Drawing Page(s)

LN.CNT 1427

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to selective anxiolytic therapeutic agents which allow for the treatment of anxiety-related disorders with less severe side-effects, such as sedative and amnesic effects, and in particular, dependence liability. These selective agents selectively or preferentially bind the  $\alpha_2$ -GABA.sub.A receptor, as compared to the  $\alpha_1$ -GABA.sub.A receptor. Alternatively, these selective agents selectively or preferentially activate the  $\alpha_2$ -GABA.sub.A receptor, as compared to the  $\alpha_1$ -GABA.sub.A receptor. The present invention also relates to methods for identifying such selective anxiolytic therapeutic agents. The present invention also relates to methods for identifying a molecule that decreases binding of a benzodiazepine to the  $\alpha_1$ -GABA.sub.A receptor, but not substantially to the  $\alpha_2$ -GABA.sub.A receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 7 OF 11 USPATFULL on STN

AN 2002:48606 USPATFULL

TI Irrigation solution and method for inhibition of **pain** and inflammation

09567863

IN Demopulos, Gregory A., Mercer Island, WA, UNITED STATES  
Pierce-Palmer, Pamela, San Francisco, CA, UNITED STATES  
Herz, Jeffrey M., Mill Creek, WA, UNITED STATES  
PA Omeros Medical Systems (U.S. corporation)  
PI US 2002028798 A1 20020307  
AI US 2001-839633 A1 20010420 (9)  
RLI Continuation-in-part of Ser. No. WO 1999-US24625, filed on 20 Oct 1999,  
UNKNOWN Continuation-in-part of Ser. No. WO 1999-US24672, filed on 20  
Oct 1999, UNKNOWN Continuation-in-part of Ser. No. WO 1999-US24558,  
filed on 20 Oct 1999, UNKNOWN Continuation-in-part of Ser. No. WO  
1999-US24557, filed on 20 Oct 1999, UNKNOWN Continuation-in-part of Ser.  
No. WO 1999-US26330, filed on 5 Nov 1999, UNKNOWN Continuation-in-part  
of Ser. No. US 1998-72913, filed on 4 May 1998, UNKNOWN Continuation of  
Ser. No. US 1996-670699, filed on 26 Jun 1996, UNKNOWN  
Continuation-in-part of Ser. No. WO 1995-US16028, filed on 12 Dec 1995,  
UNKNOWN Continuation-in-part of Ser. No. US 1994-353775, filed on 12 Dec  
1994, ABANDONED  
PRAI US 1998-105026P 19981020 (60)  
US 1998-105029P 19981020 (60)  
US 1998-105044P 19981020 (60)  
US 1998-105166P 19981021 (60)  
US 1998-107256P 19981105 (60)  
DT Utility  
FS APPLICATION  
LREP CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC, 1420 FIFTH AVENUE, SUITE  
2800, SEATTLE, WA, 98101-2347  
CLMN Number of Claims: 19  
ECL Exemplary Claim: 1  
DRWN 12 Drawing Page(s)  
LN.CNT 4713

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and solution for perioperatively inhibiting a variety of  
**pain** and inflammation processes at wounds from general surgical  
procedures including oral/dental procedures. The solution preferably  
includes at least one pharmacological agent selected from the group  
consisting of a mitogen-activated protein kinase (MAPK) inhibitor, an  
.alpha..sub.2-receptor agonist, a neuronal nicotinic acetylcholine  
receptor agonist, a cyclooxygenase-2 (COX-2) inhibitor, a soluble  
receptor and mixtures thereof, and optionally additional multiple  
**pain** and inflammation inhibitory agents at dilute concentration  
in a physiologic carrier, such as saline or lactated Ringer's solution.  
The solution is applied by continuous irrigation of a wound during a  
surgical procedure for preemptive inhibition of **pain** and while  
avoiding undesirable side effects associated with oral, intramuscular,  
subcutaneous or intravenous application of larger doses of the agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 8 OF 11 USPATFULL on STN  
AN 2002:209546 USPATFULL  
TI Arylhydantoin derivatives and uses thereof  
IN Hoffman, Jacob M., Lansdale, PA, United States  
Bock, Mark G., Hatfield, PA, United States  
DiPardo, Robert M., Lansdale, PA, United States  
Payne, Linda S., Lansdale, PA, United States  
Patane, Michael A., Harleysville, PA, United States  
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)  
PI US 6436962 B1 20020820  
AI US 2000-671518 20000927 (9)  
PRAI US 1999-156753P 19990930 (60)  
DT Utility  
FS GRANTED

09567863

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Patel, Sudhaker B.

LREP Brown, Baerbel R., Walton, Kenneth R., Fitch, Catherine D.

CLMN Number of Claims: 31

ECL Exemplary Claim: 1

DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

LN.CNT 2793

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Arylhydantoin derivatives and their pharmaceutically acceptable salts are disclosed. The synthesis of these compounds and their use as alpha 1a adrenergic receptor antagonists is also described. One application of these compounds is in the treatment of benign prostatic hyperplasia. These compounds are typically selective in their ability to relax smooth muscle tissue enriched in the alpha 1a receptor subtype without at the same time inducing hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the instant compounds is to provide acute relief to males suffering from benign prostatic hyperplasia, by permitting less hindered urine flow. Another utility of the instant compounds is provided by combination with a human 5-alpha reductase inhibitory compound, such that both acute and chronic relief from the effects of benign prostatic hyperplasia can be achieved.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 9 OF 11 USPATFULL on STN

AN 2001:67672 USPATFULL

TI Dihydropyrimidines and uses thereof

IN Nagarathnam, Dhanapalan, Ramsey, NJ, United States

Wong, Wai C., Newark, NJ, United States

Miao, Shou Wu, Edison, NJ, United States

Gluchowski, Charles, Wayne, NJ, United States

Patane, Michael A., Harleysville, PA, United States

PA Synaptic Pharmaceutical Corporation, Paramus, NJ, United States (U.S. corporation)

PI US 6228861 B1 20010508

WO 9717969 19970522

AI US 1998-68782 19981110 (9)

WO 1996-US18573 19961115

19981110 PCT 371 date

19981110 PCT 102(e) date

RLI Continuation-in-part of Ser. No. WO 1995-US15025, filed on 16 Nov 1995

Continuation-in-part of Ser. No. US 1996-648770, filed on 16 May 1996, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak R.

LREP White, John P. Cooper & Dunham LLP

CLMN Number of Claims: 21

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2014

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention is directed to dihydropyrimidine compounds which are selective antagonists for human .alpha..sub.1A receptors. This invention is also related to uses of these compounds for lowering intraocular pressure, inhibiting cholesterol synthesis, relaxing lower urinary tract tissue, the treatment of benign prostatic hyperplasia, impotency, cardiac arrhythmia and for the treatment of any disease where the antagonism of the .alpha..sub.1A receptor may be useful. The invention further provides a pharmaceutical composition comprising a therapeutically effective amount of the above-defined compounds and a pharmaceutically acceptable carrier.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 10 OF 11 USPATFULL on STN  
AN 2001:4740 USPATFULL  
TI Dihydropyrimidines and uses thereof  
IN Nagarathnam, Dhanapalan, Ramsey, NJ, United States  
Wong, Wai C., Newark, NJ, United States  
Miao, Shou Wu, Edison, NJ, United States  
Patane, Michael A., Harleysville, PA, United States  
Gluchowski, Charles, Danville, CA, United States  
PA Synaptic Pharmaceutical Corporation, Paramus, NJ, United States (U.S. corporation)  
PI US 6172066 B1 20010109  
AI US 1997-858061 19970516 (8)  
PRAI US 1996-17582P 19960516 (60)  
DT Patent  
FS Granted  
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Balasuhramanian, Vankataraman  
LREP White, John P. Cooper & Dunham LLP  
CLMN Number of Claims: 19  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 1732

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention is directed to dihydropyrimidine compounds which are selective antagonists for human  $\alpha_{1A}$  receptors. This invention is also related to uses of these compounds for lowering intraocular pressure, inhibiting cholesterol synthesis, relaxing lower urinary tract tissue, the treatment of benign prostatic hyperplasia, impotency, cardiac arrhythmia and for the treatment of any disease where the antagonism of the  $\alpha_{1A}$  receptor may be useful. The invention further provides a pharmaceutical composition comprising a therapeutically effective amount of the above-defined compounds and a pharmaceutically acceptable carrier.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 11 OF 11 USPATFULL on STN  
AN 2000:54133 USPATFULL  
TI Alpha 1a adrenergic receptor antagonists  
IN Patane, Michael A., Harleysville, PA, United States  
Bock, Mark G., Hatfield, PA, United States  
Nagarathnam, Dhanapalan, Ramsey, NJ, United States  
Lagu, Bharat, Maywood, NJ, United States  
Wong, Wai C., Newark, NJ, United States  
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)  
Synaptic Pharmaceutical Corp., Paramus, NJ, United States (U.S. corporation)  
PI US 6057350 20000502  
AI US 1998-98781 19980617 (9)  
PRAI US 1997-50136P 19970618 (60)  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Stockton, Laura L.  
LREP Walton, Kenneth R., Winokur, Melvin  
CLMN Number of Claims: 24  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 2143

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

09567863

AB This invention relates to certain novel compounds and derivatives thereof, their synthesis, and their use as alpha 1a adrenergic receptor antagonists. One application of these compounds is in the treatment of benign prostatic hyperplasia. These compounds are selective in their ability to relax smooth muscle tissue enriched in the alpha 1a receptor subtype without at the same time inducing hypotension. One such tissue is found surrounding the urethral lining. Therefore, one utility of the instant compounds is to provide acute relief to males suffering from benign prostatic hyperplasia, by permitting less hindered urine flow. Another utility of the instant compounds is provided by combination with a human 5-alpha reductase inhibitory compound, such that both acute and chronic relief from the effects of benign prostatic hyperplasia are achieved.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 13:16:58 ON 10 SEP 2003)

FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 13:17:21 ON 10 SEP 2003

L1 4 S SAPORIN AND IMILOXAN  
L2 0 S L1 AND ADRENERGIC RECEPTOR?  
L3 189 S SAPORIN AND ADRENERGIC RECEPTOR  
L4 2 S L3 AND PRAZOSIN  
L5 0 S L1 AND ADREN? (4A) RECEPTOR?  
L6 13375 S THERAP? AND ADREN? (4A) RECEPTOR?  
L7 665 S L6 AND ALPHA? (5A) SUBTYPE?  
L8 329 S L7 AND TARGET?  
L9 1 S L8 AND TARGET? (5A) BIND? (5A) ALPHA?  
L10 122 S L8 AND TARGET? (7A) ALPHA?  
L11 66 S L10 AND PRAZOSIN  
L12 2 S L11 AND ARC 239  
L13 2305 S ALPHA? 2 (5A) SUBTYPE?  
L14 1 S L13 AND TARGET? (7A) BIND? (5A) ALPHA?  
L15 662 S L13 AND BIND? (6A) ALPHA?  
L16 186 S L13 AND BIND? (4A) ALPHA? (4A) RECEPTOR?  
L17 15 S L16 AND PAIN  
L18 14 S L17 NOT L14  
L19 14 DUP REM L18 (0 DUPLICATES REMOVED)  
L20 11 S L19 AND ALPHA (3A) 2B  
L21 11 DUP REM L20 (0 DUPLICATES REMOVED)

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